

Formulation and Evaluation of Ascorbic Acid Mouth Dissolving Tablets

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ABSTRACT

Mouth dissolving tablet have better accessibility and tolerability for patients, mouth dissolving tablet is the most essential and recommended way of drug delivery. One more difficulty can be solved by administering the new drug with the mouth dissolving tablet formulation so that the drug quickly dissolves and breaks in the mouth in fewer minute due to the effect of super disintegrating agents that maximize the pore structure of the formulation. The purpose of this research work was to develop mouth-dissolving tablet of Ascorbic Acid. Tablet containing drug and excipients were prepared by direct compression method. Excipients in combinations were merged to achieve the aim. Effect of different combinations was studied to optimize the best formulation. Drug excipients interaction studies were carried out by FTIR spectral analysis. The tablets were evaluated for their hardness, disintegrating time, wetting time, and dissolution parameters. It was determined that the tablets having the combination of Crospovidone, Croscarmellose sodium, and microcrystalline cellulose fulfilled all the evaluation parameters and thus selected as the optimized formulation. Optimized formulation was undergone for stability testing as a parameter to expect the shelf life. The major role produced by the superdisintegrant and inactive substances for improving the bioavailability of drug and advances the drug release in the oral cavities.

Keywords: Ascorbic acid; Mouth dissolving tablet; Optimized formulation; Superdisintegrants; Improved bioavailability; Excipients; Dissolution; Disintegration; Wetting time; Oral drug delivery system.

1. Introduction

In spite of important innovations in delivery of drug, the oral pathway is quiet the greatest standard method to administer satisfying agents since of its exact dosage, inexpensive therapy, self-medicated, non-invasive (in the cavity) manner, and comfort administration, which all give to great patient comfort. This particular formulation segment is intended specifically for patients who are dysphasic, elderly, young, bedridden, or psychotic and who either cannot or will not swallow traditional oral formulations. All mouth dissolving tablets that have been permitted as orally disintegrating tablets classify according to Food and Drug Administration (FDA). A tablet which melts in the mouth in fewer minutes before swallowing is bring up as mouth dissolving tablet by the European Pharmacopeia [1–5]. Up to 50–60% of all dose forms are commonly considered as being the traditional forms (tablet and capsule). Tablet is unique medicated dosage form, prepared from an excipient, which is known as inactive ingredient and active ingredient mixture that is frequently in powder form and is compressed into a solid dosage. For confirming and improving the effective tableting, the excipients may include diluents, binders or granulating agents, glidants (flow supports) and lubricants; superdisintegrants to improve disintegration; sweeteners or flavors to enhance taste; and pigments to provide the tablets color. The results of these recent studies specify that over 50% of people select mouth dissolving tablets as compared to other dosage forms. The use of superdisintegrants (Croscarmellose, crospovidone, and sod. starch glycolate) is the first method which is used for the preparation of mouth dissolving tablets. Due to the cost-efficiency, speed, and effectiveness, the direct compression method is most suggested method of formulating the tablets. It is possible to turn numerous medications into mouth dissolving tablets. The rate of drug absorption is impacted by the substance's speed of solubility. The therapeutic action happen more quickly, as the absorption starts and the drug dissolves faster into the solution. In saliva, tablet should typically dissolve or break down freely in less than 60 seconds, or 50–60 seconds

[6–13]. Mouth dissolving tablets dissolve or disintegrate in the oral cavity without the need for water and contain substances that mask the unpleasant taste of the active ingredients. That masked active component is then absorbed by the patient's saliva together with soluble and insoluble excipients.

It was concluded that dissolution depends on absorption or you can say faster dissolution, faster absorption (only non-ionized form of the drug) and activity. Some drugs are absorbed from the oral cavity, pharynx and esophagus when saliva enters the stomach. Thus, the bioavailability of the drug is significantly higher than in conventional tablet dosage forms. Mouth dissolving tablets usually take less than 1 minute or 60 seconds to disintegrate [14,15].

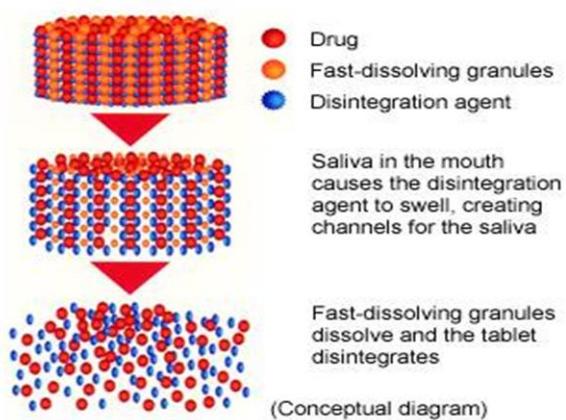


Figure 1. Method of disintegration of Mouth Dissolving Tablet

Ascorbic acid is a water-soluble vitamin that is good for growth and repair in all parts of the body. It helps the body produce collagen, an important protein used to build skin, cartilage, tendons, ligaments and blood vessels. Ascorbic acid is important for the healing and repair and maintenance of bones and teeth. Low levels of ascorbic acid have been linked to several conditions, including increased blood pressure, gallbladder disease, stroke, some cancers. The importance of vitamins as drugs is the prevention and treatment of several diseases. Vitamins are not naturally synthesized in the body, a balanced diet will maintain the levels of these vitamins. But sometimes you can get sick with your diet with these vitamins. For these conditions, multivitamins are available in the market to provide adequate vitamins [16,17].

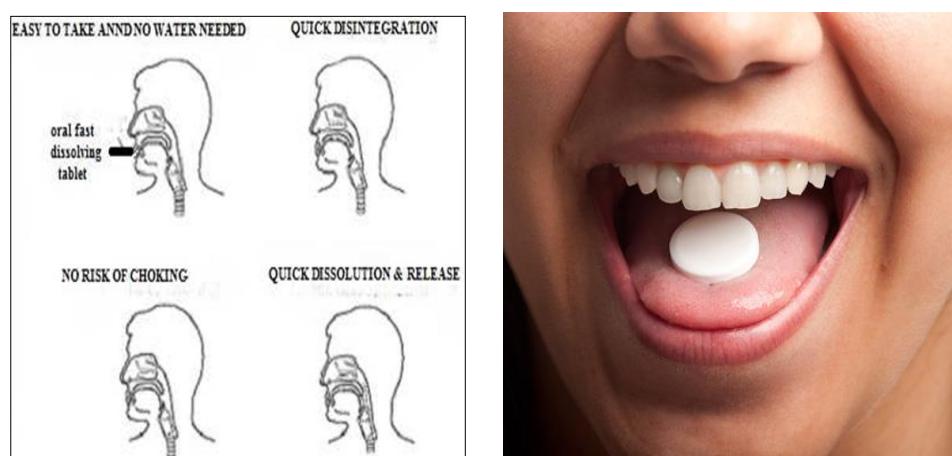


Figure 2. Administration of Mouth dissolving Tablets

1.1. Study Objectives

- ❖ The concept of MDT system is to deliver the patient with conventional means of capturing their medication.
- ❖ Drugs are absorbed from the mouth, pharynx, and esophagus as saliva permits down into the stomach.
- ❖ In this current study effort will be made to formulate a patient friendly dosage form of mouth dissolving tablet of Ascorbic acid.
- ❖ Obviating the need of water for the administration of the tablet.
- ❖ The bioavailability of the drug is suggestively higher than the detected conventional tablet dosage form.
- ❖ The MDTs have the property of fast disintegration and fast release of drug as they come in contact with saliva.

2. Material and Methods

2.1. Materials

Ascorbic acid as a sample purchased from FINE – CHEM Ltd. (Mumbai) Crospovidone and Croscarmellose sodium from Akhil Healthcare Pvt. Ltd. (Vadodara), Microcrystalline Cellulose from Himedia Laboratories Pvt. Ltd. (Mumbai), Magnesium Stearate from Central Drug House Pvt. Ltd. (New Delhi), and Mannitol from RFCL Limited (New Delhi). Distilled water has taken from the Department of Pharmacy. All the chemicals used were of analytical grade.

Table 1. Purpose of Ingredients for Mouth Dissolving Tablet of Ascorbic Acid

Ingredient	Purpose
Ascorbic acid	Active Pharmaceutical Ingredient
Microcrystalline cellulose	Binder
Crospovidone	Superdisintegrant
Croscarmellose Sodium	Superdisintegrant
Mannitol	Diluent
Magnesium stearate	Glidant
Aspartame	Sweetener

3. Experimental Work

3.1. Drug-Excipient Compatibility Studies

The drug (Ascorbic acid) compatibility studies with the excipients was finished by mixing ascorbic acid with microcrystalline cellulose, crospovidone, magnesium stearate and mannitol with using differential scanning calorimeter. In a transparent glass sample bottle, add 1gram amount of ascorbic acid mixed with 1 gram of each of the excipients. Then, in a small aluminum pan 1 mg mixture was packed carefully sealed and scanned with black

pan. This process was repeated for each of the component alone and achieved thermograms were compared from the ascorbic acid.

3.1.1. Fourier transforms infrared (FT-IR) spectral analysis

FTIR is used to identify the functional group of a molecule. The drug is mixed with a potassium bromide disk that was scanned at 4 mm/s with a resolution of 2 cm at a wavenumber range of 400-4000/cm in the preparation of mouth dissolving tablets. The instability of the drug caused by the interaction of drug and polymer. Pre-formulation studies of drug-polymer interaction are very important in selecting suitable polymers. FTIR spectroscopy was used to determine the compatibility of selected polymers. The drug and the combination of the drug with the polymer were look over individually.

3.1.2. Differential Scanning Calorimetry (DSC) analysis

Differential Scanning Calorimetric measurement of ascorbic acid was performed with an instrument (DSC 60+ Shimadzu Japan) to measure the thermotropic transition. An empty aluminum pan was used for comparison and the samples were carefully placed in alternative aluminum pan. The measurement was completed at a temperature range of 30°C to 305°C at a rate of 10°C per minute in a non-reactive (reactive) atmosphere.

3.2. Precompression Parameters [18–24]

➤ Angle of repose

To discover the angle of repose, can measure the friction forces in a loose powder θ . It is well-defined as the largest possible angle that may be produced between the surface of the powder pile and the horizontal. The angle of repose is measured by using technique termed as Newman's funnel. The amount which is measured, put into the funnel. The funnel is placed such that the tip just fixes the blend heap at the top. The mixture is acceptable to flow freely through the funnel on the outside.

$\text{Tan } (\theta) = h/r$, θ = angle of repose, r = radius of the cone base, h = height of the cone.

➤ Bulk density

Bulk density (D_b) is the mass of the powder divided by the bulk volume. It is denoted by the unit g/cm^3 . The ultimate step is to assess the bulk density by dividing the sample weight in grams by the complete volume in cubic centimeters.

$\text{Bulk density} = M / V_b$, V_b = Powder bulk volume, M = mass of powder in gram.

➤ Tapped density

By dividing the overall mass of the powder by the tap volume, its tap density can be calculated. This can be measured by adding a measuring cylinder of mass to the drug-excipient arrangement. A cylinder is suitable to fall naturally from a height of 10 cm onto a hard surface every 2 seconds. Settlement continues until the difference between Consecutive dimensions is less than 2 percent. It is stated in grams/ml.

$\text{Tapped density} = M/V_t$, V_t = volume of the tapped packing. M = mass of powder.

➤ Compressibility indices

This is the tendency of the powder to compact. It is measured with a thread density device for 500, 750 and 1250 needles with a change of no extra than 2 percent. Based on the superficial bulk density and tap density, the compressibility of the powder mixture was measured in percent by means of the formula.

% Compressibility = (Tapped density - Bulk density) / Tapped Density x 100.

➤ Hausner's ratio

The Hausner's ratio is defined as a number that correlates with the flow ability of a powder or granular material. From the bulk Hausner's ratio and bulk densities was calculated using the following formula.

Hausner's ratio = Tapped density / Bulk density.

Table 2. Standard value of Angle of Repose and Compressibility index

Flow Property	Angle of Repose	Compressibility index
Excellent	25-30	<10
Good	31-35	11-15
Fair	36-40	16-20
Passable	41-45	21-25
Poor	46-55	26-31
Very poor	56-65	32-37
Very very poor	>66	>38

3.3. Formulation of Ascorbic Acid MDTs

The Mouth dissolving tablet of Ascorbic acid was prepared by using the Direct Compression process. Using a mortar and pestle, a powder blend of the medication, direct compression excipient (without lubricant; magnesium stearate), and glidant (talc) was evenly combined for five minutes. Following that, the lubricant and glidant were added in the prescribed amounts, and mixing lasted for an extra five minutes. The tableting was done at different compression loads using a single punch tableting machine that was equipped with 12mm normal concave facing punches. The weight of the desired pill was 200 mg.

Direct compression is usually performed on a crystalline material with good properties such as flow ability, compressibility, etc. Direct pressing has important advantages such as time saving, cost efficiency and operational safety. Sieve the ascorbic acid, mannitol through a 40 mm mesh using a geometric mixer and sieve the microcrystalline cellulose, crospovidone and mannitol through a 40 mm mesh and the above mixture for 5 minutes. After passing the magnesium stearate through a 40 mm mesh, add the above mixture for 2 minutes. Finally, the mixture should be compressed into tablets in a single-rotator punch machine [25].



Figure 3. Schematic procedure of Mouth Dissolving Tablets

Table 3. Composition of Formulation of Mouth Dissolving Tablet

S. No.	Constituents (mg)	F1	F2	F3	F4	F5	F6
1	Ascorbic acid	20	20	20	20	20	20
2	Crospovidone	4	6	8	-	-	-
3	Croscarmellose Sodium				4	6	8
4	Microcrystalline Cellulose	152	150	148	152	150	148
5	Mannitol	15	15	15	15	15	15
6	Magnesium stearate	5	5	5	5	5	5
7	Aspartame	4	4	4	4	4	4
Total		200	200	200	200	200	200

3.4. Post Compression Parameters

Post-compression inspection is essential for manufactured tablets. These parameters are like brittleness, hardness, weight variation, appearance and thickness. Every evaluated parameters for all dosage forms are presented in the table. The common look of the tablet was visually examined for odor, color, shape, and texture [26–33].

➤ **Thickness:** By using a Vernier caliper, tablet thickness was calculated. The tablet was positioned upright between the two oral cavity and the width was measured and 6 tablets were used for this research and articulated in millimeters.

➤ **Weight variation:** The weight change test is performed by balancing 20 medicines separately, computing the average weight and equating the weight of the individual tablet with the average. The weight change test would be a pleasing way to determine the uniformity of the drug content of the tablets.

➤ **Hardness:** Hardness is also called tablet crushing strength. Using a Monsanto hardness tester the tablet hardness was analyzed. The tablet was sited laterally between the upper and lower pistons and power was applied by turning the threaded bolt until the tablet broke and the tablet hardness was measured in kg/cm².

➤ **Friability:** This is determined by the Roche friabilator by subjecting several tablets to a combination of friction and impact using a plastic chamber that rotates at 25 rpm, dropping the tablet 100 revolutions of an inch away. The pre-weighed tablets were powdered and reweighed, and according to the standard limit, friability should be less than 1%. It is calculated using the formula.

$$\% \text{ Friability} = \text{Initial weight} - \text{Final weight} / \text{Initial weight}$$

➤ **In vitro drug release:** By using USP Dissolving Apparatus II dissolution profile of the tablet was determined at 37 ± 0.5 °C with stirring at 75 rpm in 900 mL of simulated gastric fluid (0.1 N HCl). Several samples were taken with the same volume of replacement-simulated fluid at 10, 20, 30, 40, 50 and 60 minutes. Samples were sieved using Whatman filter paper and absorbance was occupied using an ultraviolet spectrophotometer and calibration curve.

➤ **Wetting time:** The irrigation time and the contact angle of the dosage form are related. This must be evaluated to explain the disintegrating properties of tablet; a shorter wetting time means the tablet disintegrates faster. This is achieved by placing the tablet in a small petri dish with an inner diameter of 6.5 cm, adding 6 ml of water and calculating how long it takes the tablet to stay wet.

➤ **Disintegration test:** The disintegration times of fast dissolving pills must be adjusted because they must dissolve without water to ensure accuracy of the test. In the 10 cm of Petri dish, 10 ml of water is placed. The tablet is carefully placed in the middle of the Petri dish and it is likely to observe how long it takes to finally crumble into small pieces.

➤ **General appearance:** Customers' perceptions of a tablet's overall appearance, visual identity, and "elegance" are influenced by its size, shape, and color, as well as taste, surface texture, physical defects, consistency, and legibility of identification marks.

➤ **Size and shape:** The size and shape of the tablet may be accomplished and tracked in terms of its measurements.

4. Result and Discussion

4.1. Drug-Excipient Compatibility Study

4.1.1. Fourier-transforms infrared spectral analysis

The sample IR was interpreted and matched with reference IR spectrum is presented in figure. The obtained IR spectra of drug material (Ascorbic acid) and polymer (Microcrystalline cellulose) showed the prominent peaks interaction (3312.54cm^{-1} , 2981.73cm^{-1} , 1753.72cm^{-1} , 1316.76cm^{-1} and 1024.06cm^{-1}) of functional group existing in the drug and polymer sample which ascertained the purity of drug and polymer.

This study showed that the sample of drug taken was authentic. The sample IR was interpreted and matched with reference IR spectrum is given in figure. The obtained IR spectra of drug showed the prominent peaks interaction

(1652.06^{cm⁻¹}, 1022.99^{cm⁻¹}, 1313.32^{cm⁻¹} and 754.11^{cm⁻¹}) of functional group existing in the drug sample which ascertained the purity of drug. This study showed that the sample of drug taken was authentic. The sample IR was interpreted and matched with reference IR spectrum is given in figure.

The obtained IR spectra of polymer showed the prominent peaks interaction (3272.07cm^{-1} , 1588.61cm^{-1} , 1017.57cm^{-1} and 570.06cm^{-1}) of functional group existing in the polymer sample which ascertained the purity of polymer. This study showed that the sample of polymer taken was authentic

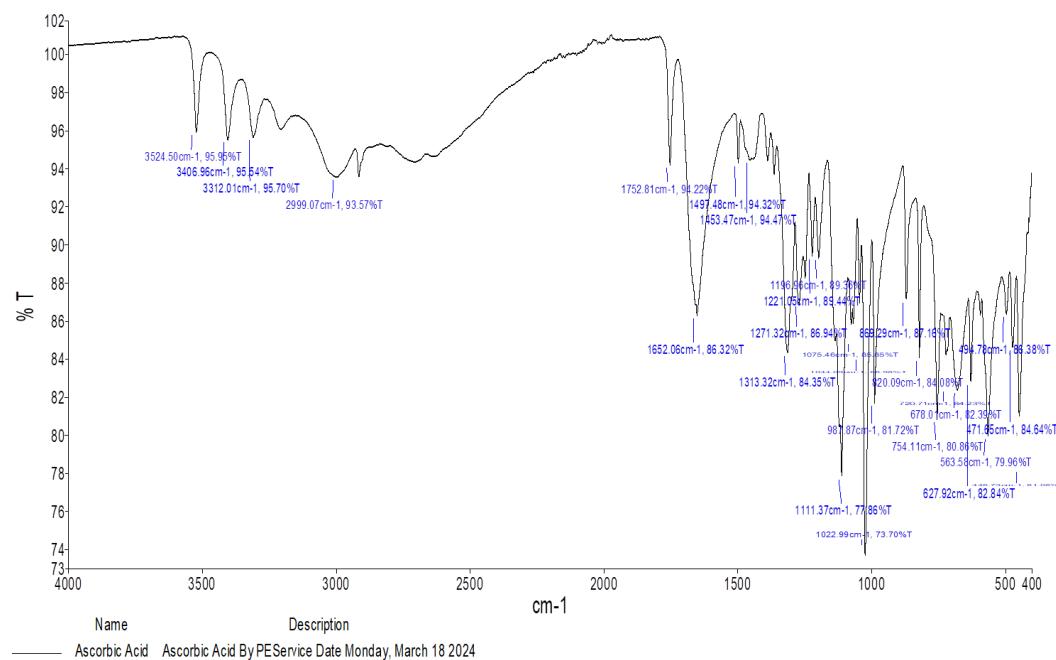


Figure 4. Fourier Transform Infrared Spectroscopy (FTIR) of Pure Ascorbic Acid

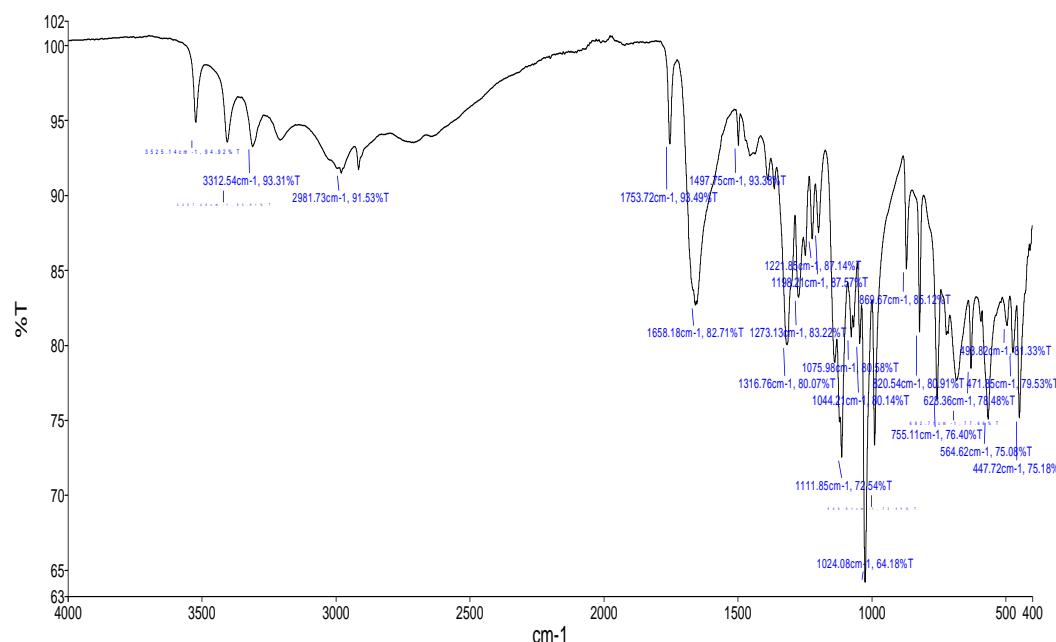


Figure 5. Fourier Transform Infrared Spectroscopy (FTIR) of Ascorbic acid + microcrystalline cellulose

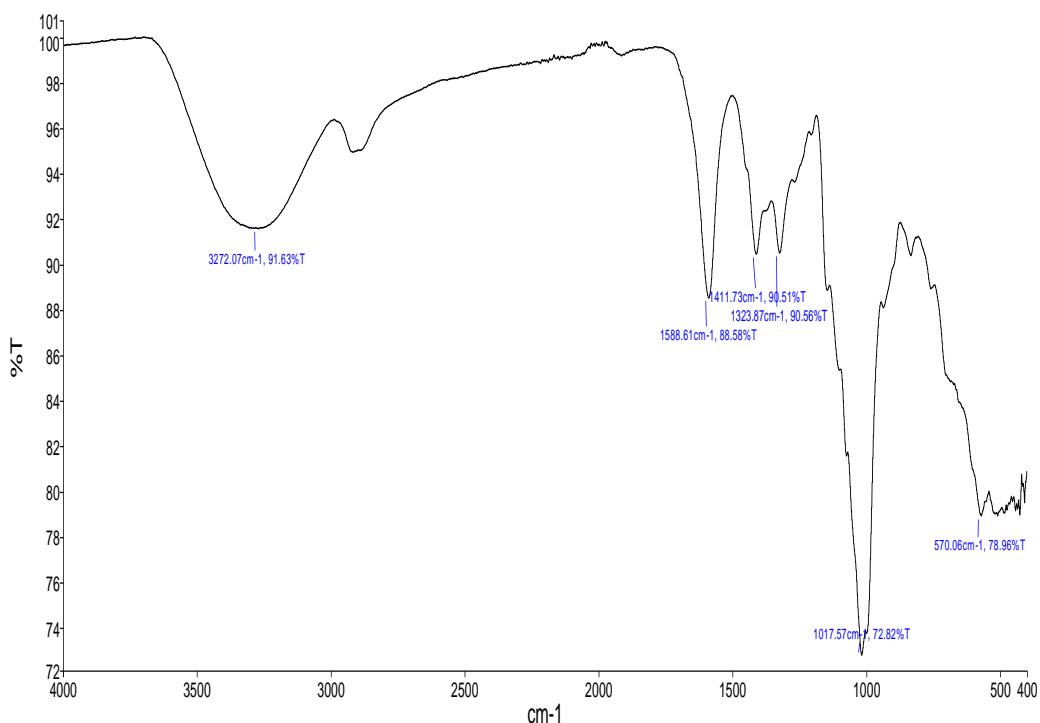


Figure 6. Fourier Transform Infrared Spectroscopy (FTIR) of microcrystalline cellulose

4.1.2. Differential Scanning Calorimetry

The DSC of clean drug (Ascorbic acid) showed an endothermic sharp peak 194.99°C corresponding to its narrow melting range and crystalline nature. The normal melting range of the drug is 190 °C to 200°C and this graph depicts the exact melting point 194°C.

The DSC of pure polymer (Microcrystalline cellulose) displayed a sharp endothermic peak 77.78°C parallel to its narrow melting range and crystalline nature. The normal melting range of the drug is 76°C to 78°C and this graph depicts the exact melting point 77.78°C.

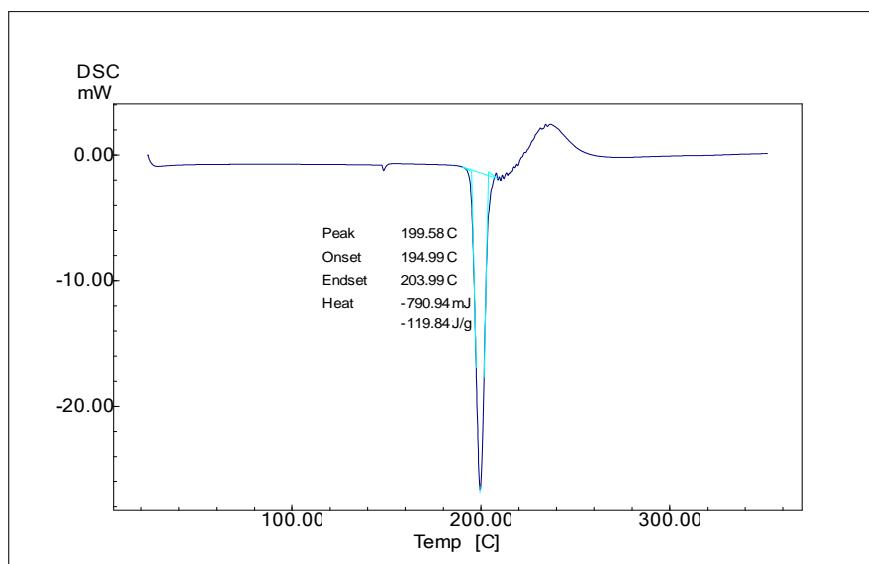


Figure 7. Differential Scanning Curve (DSC) of Ascorbic Acid

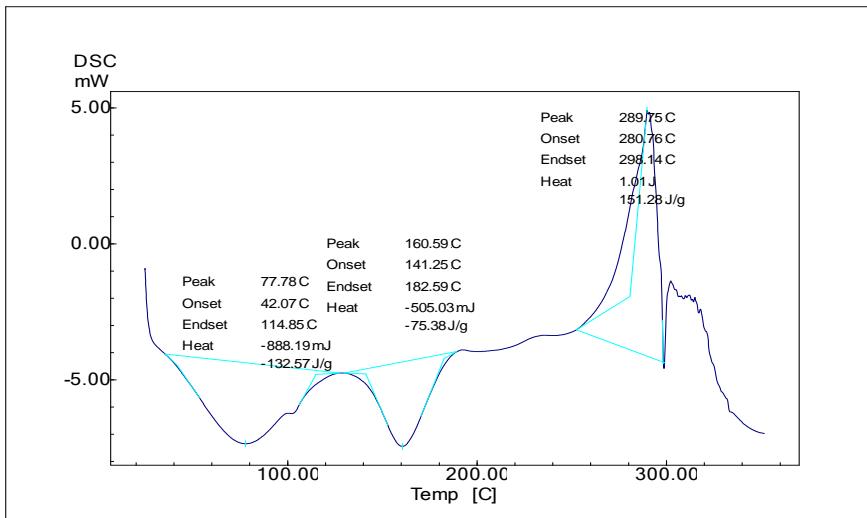


Figure 8. Differential Scanning Curve (DSC) of Microcrystalline Cellulose

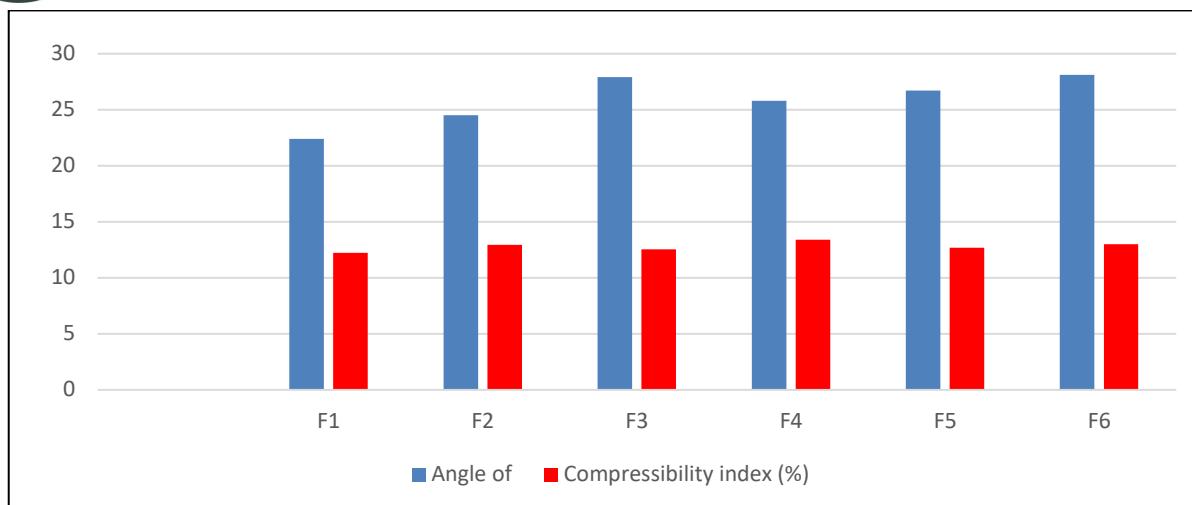
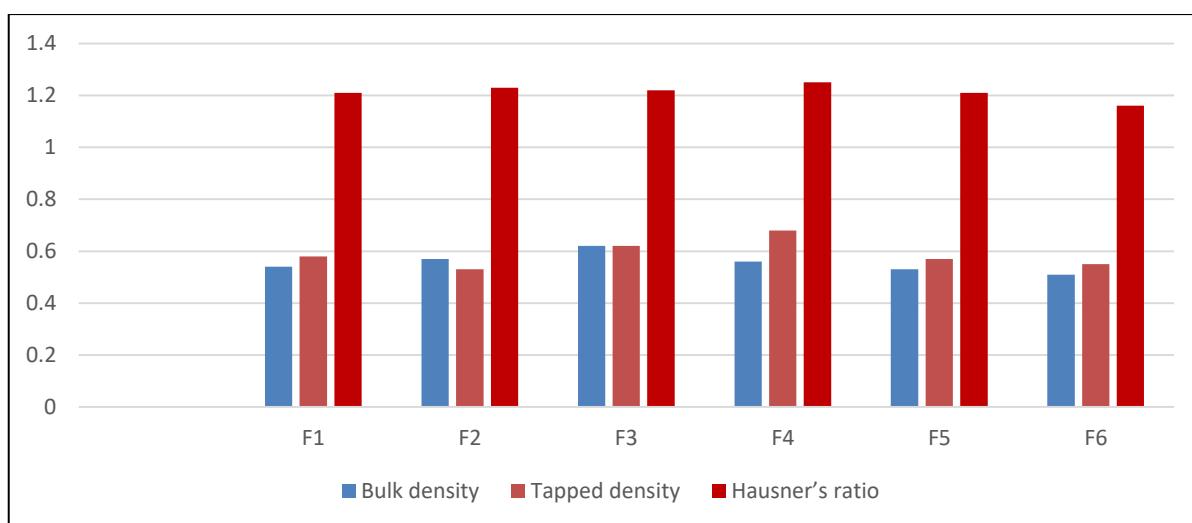
Tablets were examined for Friability (Roche friabilator), hardness (Monsanto hardness test) weight uniformity (Denver Instrument) and drug content estimation (UV-visible spectrophotometer) using a calibration curve. The dissolution test was performed according to USP, speed 75 rpm, temperature 37 °C, in 0.1 M HCL. The amount of drug release was measured at 10, 20, 30, 40, 50 and 60 min intervals and determined with a UV-visible spectrophotometer using a calibration curve.

4.2. Evaluation of Precompression Parameters

The vital parameter in the compressibility of powder is bulk density. Bulk density was found between 0.51 to 0.62 g / cm³. Another one is tapped density of the powder and it was 0.53 to 0.68 g/cm³. The powder flow is correlated with the angle of repose. The range between 25-30 indicates admirable flow ability, while poor flow ability indicates above 45. In between 31-35 specifies good flow. The angle of repose was detected between 22.4 and 28.1 g/cm³. The indicator of the compressibility is Carr's index. The 21% value displays fair to passable compressibility. It was found to be 12.22 to 13.38. The parameter describing flow characteristics is Hausner's ratio. It indicates the good flow below 1.43, while indicates poor flow above the range of 1.43. It turned out to be 1.16-1.25.

Table 4. Pre-compression Parameters of Powder Blend

S. No.	Formulation	Angle of repose	Bulk density	Tapped density	Compressibility index (%)	Hausner's ratio
1	F1	22.4	0.54	0.58	12.22	1.21
2	F2	24.5	0.57	0.53	12.92	1.23
3	F3	27.9	0.62	0.62	12.53	1.22
4	F4	25.8	0.56	0.68	13.38	1.25
5	F5	26.7	0.53	0.57	12.67	1.21
6	F6	28.1	0.51	0.55	13.00	1.16


Figure 9. Compressibility Index and Angle of Repose

Figure 10. Tapped density, Bulk density and Hausner's ratio

4.3. Postcompression Parameters of Tablets

Table 5. Evaluation Parameters of different formulations

Formulation	Weight variation %	Thickness (mm)	Hardness (Kg/cm ²)	Friability
F1	3.2	5.18	3.20	0.72
F2	3.5	5.46	3.13	0.68
F3	3.8	5.22	3.50	0.61
F4	4.1	5.58	4.01	0.75
F5	3.7	5.45	3.72	0.66
F6	4.2	5.71	3.35	0.82

Formulation	Disintegration time (sec)	Wetting time (sec)	% Drug content
F1	28.35	32.22	95.57
F2	30.25	30.13	97.00
F3	25.31	34.28	97.67
F4	28.02	38.72	98.27
F5	32.54	36.01	99.52
F6	35.69	37.08	98.64

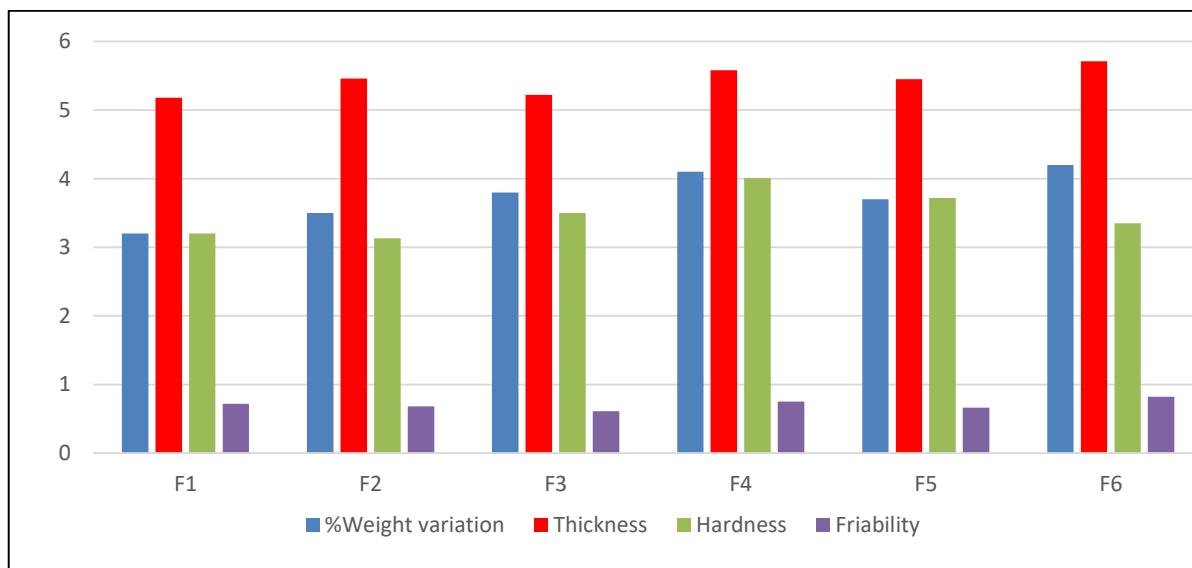


Figure 11. Thickness, Hardness, % Weight variation and Friability

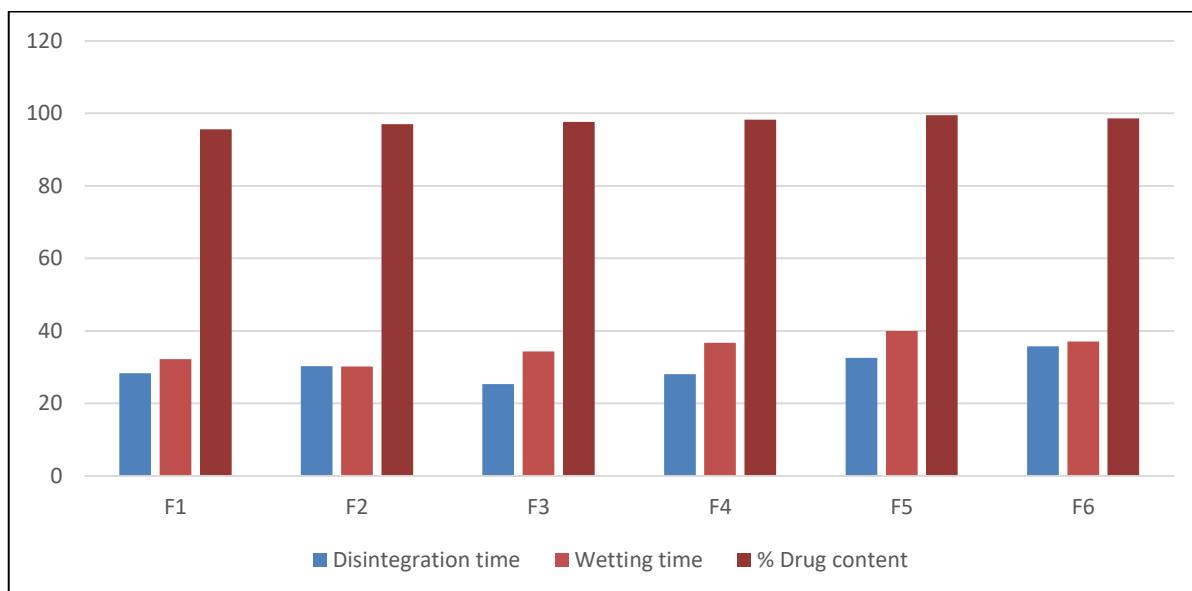


Figure 12. Wetting time, Disintegration time and % Drug content

5. Conclusion

The mouth dissolving tablet quickly enhancing the acceptance as it produces comfort to the patients. As the formulation required the small quantity of active pharmaceutical ingredient to formulate. Hence, the absorption, disintegration and bioavailability of the tablet rise quickly. It enhances the therapeutic effect and absorb rapidly through the buccal cavity or mucosal membrane of the mouth.

According to the above investigation, the mouth dissolving tablet that was compressed using the direct compression method produced a result that was both satisfactory and acceptable. The medicine releases from the tablet instantly because of the direct compression process. Based on the before mentioned research, it was determined that the mouth dissolving tablet formulation that reduces side effects and enhances good effects on the body while promoting patient compliance is the most successful. The outcomes from each batch, ranging from formulation 1 through formulation 6. Formulation 5 yielded the best results for the angle of repose, Carr's index, Hauser's ratio, and superior flow ability when compared to batches. Given that it produced more than 80% uniform results, formulation F5 stood out among the before mentioned formulation batches as our top pick for additional development of a product with commercial potential.

6. Future Prospects

With many pharmaceutical advantages such as better efficacy compared to conventional mouth dissolving tablets. For example, they require less active ingredient to be effective, promote absorption profiles and provide better bioavailability of drugs than conservative tablets and capsules. There are still many areas of development for orally soluble tablet preparations. Most of the gold disintegrating tablets on the market have a reasonable disintegration, for example less than minutes, but the absolute development is improving. The new technique aims to increase the dose of hydrophobic drugs in larger quantities, which do not have a significant effect on oral dissolution properties. The greatest advance in mouth dissolving tablet technology is the delivery of a specific drug dose with a half-life of 12-24 hours. Such compositions would be huge, convenient and reliable. Mouth dissolving tablets require large amounts of excipients and higher drug doses and facilitate preparation.

Declarations

Source of Funding

This study did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

All the authors took part in literature review, analysis and manuscript writing equally.

Availability of data and material

All data pertaining to the research is kept in good custody by the authors.

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